

DETAILED ACTION

Applicants' arguments filed August 31, 2010 have been received and entered. Claims 1 and 25 have been amended, while claim 3 is canceled. Claims 1, 2, 4-25 are pending in the application.

Election/Restrictions

Applicant's election of Group I in the reply filed on 10/12/07 was acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election was treated as an election without traverse (MPEP § 818.03(a)).

Accordingly, claims 8, 9, 11-23 remain withdrawn from consideration for being directed to non-elected subject matter. Claims 1- 2, 4- 7, 10, 24 and 25 are currently under examination.

Withdrawn- Claim Rejections - 35 USC § 102

Claims 1, 2, 4-7, 24 were rejected under 35 U.S.C. 102(e) and claim 10 is also rejected as being anticipated by Boyce et al. (US 6863694, dated 3/8/2005, filed 7/3/2000).

In view of Applicants' amendment of base claim 1, introducing the limitation "effecting the phase change of the immobilization medium to convert the immobilization medium in solid state", to solidify the bone and immobilization medium, that is not explicitly taught by Boyce, the previous rejection is rendered moot and hereby withdrawn. Applicants' arguments with respect to the withdrawn rejections are thereby rendered moot.

Maintained-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1- 2, 4-7, 10, 24 and 25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Boyce et al (US Patent no 5,899,939, dated 5/4/1999), Dowd et al (US 5507813, dated 4/16/1996, art of record) and Aaron et al (J Histochem Cytochem. 1987 Mar;35(3):361-9).

Claims are directed to a method of making bone particles which comprises: a) at least partially immersing a quantity of bone in an immobilization medium; b) converting the immobilization medium to a solid state, thereby solidifying the immobilization medium to provide a solidified mass of bone and immobilization medium; c) subdividing the solidified mass of bone and immobilization medium to provide subdivided particles of bone; and d) separating the bone particles from the immobilization medium.

Boyce et al teach a method of subdividing a cortical section of bone from the diaphyseal region, said method comprising wetting the bone in immobilization medium water that is then solidified by freezing at -70°C followed by freeze-dried for 2 days to separate the bone particle from water. It is further disclosed that that multilayered unitary structure is then cut to provide the shape of bone implant (example 1) (limitation of claims 1, 2, 5, 7 and 10). It is noted that the divided bone are in association with water. While Boyce et al teach (a) covering a bone in water, (b) solidifying the water and bone by freezing and then (d) subsequently freeze drying to separate the bone particle from the water, but differ from claimed method by not explicitly teaching subdividing the solidified mass to provide subdivided bone particle prior to freeze drying.

Dowd et al. disclose a method for preparing the shaped osteogenic materials by (a) using a quantity of bone particles that has been demineralized, slurried in a suitable liquid, e.g., water, organic protic solvent, aqueous solution such as physiological saline, etc., and optionally containing one or more biocompatible ingredients such plasticizers (eg. Glycerol) (limitation of claims 1, 5-6, 24), that is applied to a form such as a flat sheet, mesh screen or three-dimensional mold and excess liquid is removed, e.g., by being drained away (see col. 4, lines 58-65, col. 3, lines 25-30, col. 4, line 9). The at least partially immersed demineralized bone particles are then subject to lyophilization in accordance with procedures and conditions that are well known in the art, e.g., a shelf temperature of from about -20°C to about -35°C , a vacuum of from

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about 150 to about 100 mTorr for a time of from about 4 to about 48 hours depending on the mass (see col. 5, lines 10-15, limitation of claim 7). It is noted that Dowd et al disclose that dry or hydrated article can be cut or sized (see col. 5, lines 1-27). Therefore, the teaching of Dowd embrace subdividing bone particle in association with liquid in hydrated state or subdividing the dry mass of bone and solidified medium using routine methods known in prior art. It is noted that combination of Boyce and Dowd et al teach at least partially covering or immersing a bone in an immobilization medium (b) effect a phase change of immobilization medium to convert immobilization medium to provide a slurry or gel mass of bone and immobilization medium, (c) subdividing the mass of bone and immobilization medium to provide subdivided particle of bone mass and separate bone particle by freeze drying, however, differ from claimed invention by not explicitly teaching that subdividing could be accomplished from a frozen solid block of bone and immersion medium.

However, subdividing solid mass of bone and immobilization medium to provide subdivided bone particle was known in prior art. For instance, Aaron et al teach a method of immersing the specimen surrounded by CMC or other suitable polymers into freezing to provide a solidified block of bone and immobilization medium that is subsequently subdivided using microtome. It is further disclosed that freezing immobilization medium acts as an embedding medium resulting in more efficient cutting of bone specimen (see figure 1, table 1 and page 362, col. 2, para. 1-3).

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the teachings of Boyce et al, Dowd and Aaron to modify the method of Boyce by subdividing the frozen immobilization medium and bone prior to freeze drying using the method known in art (see Dowd), as a matter of design choice, in the method of making bone particles, as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. Said design choice amounting to combining prior art elements according to known methods to yield predictable results. One of ordinary skill in the art would be motivated to do so as Aaron teaches that freezing immobilization medium act as an embedding medium resulting in more efficient cutting of bone specimen (*supra*). Other limitation of using demineralized whole bone or section would be obvious modification of the method of Boyce in view of method for preparing the demineralized bone disclosed by Dowd. One of skill in the art would have been

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expected to have a reasonable expectation of success in subdividing the solidified mass of bone and medium because the freezing immobilization medium would support and act as an embedding medium for efficient cutting of the bone particles and because the art teaches successfully subdividing frozen immersion medium and bone. Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Response to arguments

Applicants disagree with the rejection of claim 1 over Boyce et al, Dowd et al and Aaron et al, arguing that wetting is not “at least partially immersing” as claimed. Applicants argue that mere wetting of bone does not require the section be “plunged into something that cover” or “placed into”. Applicants assert that wetting is not partially immersing. Applicants further argue it is unclear how the cutting of Boyce could be carried out if bone sections are immersed in wetting fluid as it would complicate the layer cutting without any benefit. Applicants assert that deficiency of Boyce et al is not cured by the teaching of Dowd and Aaron (see page 7 and 8 of the arguments). Applicants’ arguments have been fully considered, but are not found persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants have further engaged in selective reading of the teachings of Boyce et al. to formulate the grounds for not teaching the invention. As previously indicated, Boyce et al. in describing the method teaches wetting a bone in immobilization medium (water) that is then solidified by freezing at -70°C . It should be noted that “wet” is broadly interpreted as “covered with” as per Merriam-Webster's Online Dictionary. Thus, scope of method disclose by Boyce includes covering a bone with water and then freezing the bone covering with water. It should be further noted that “at least partially immersing a quantity of bone in immobilization medium” means completely immersing the bone in immobilization medium. Thus, bone covering with water is interpreted as liquid that covers the bone as required by the claims. In this regard, Dowd et al also teach complete immersion of bone particles in water to prepare slurry of bone particle in immobilization medium (see col. 4,

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lines 60-61), that is subsequently subdivided to separate bone particles with immobilization medium. To the extent that Boyce et al. describe at least covering a quantity of bone in water and further supported by the teaching of Dowd that teaches complete immersion of bone in immobilization medium, the rejection is applicable to the instant case. Applicants' selective reading of Boyce et al. ignores the teachings of the secondary reference of Dowd. A person of skill in the art would be motivated to immerse bone at least partially in immersion medium (water) and then solidify immobilization medium and bone as Aaron provided motivation to freeze immobilization medium that acts as an embedding medium resulting in more efficient cutting of bone specimen (see Aaron et al. page 362, col. 2, para. 1).

With respect to applicants' argument of how layer cutting would be carried out if the bone is partially immersed in fluid, it should be noted Boyce teaches covering (wetting) the bone with immobilization medium (water), which is then solidifying the same by freezing at -70°C . It is Aaron who explicitly teaches immersing bone in immobilization medium and then freezing bone with immobilization medium to provide a solidified block of bone and immobilization medium that is subsequently subdivided in layers of bone tissue using microtome or other appropriate bone milling apparatus known in art (*supra*). To the extent that Aaron et al. describe the completely immersed bone in immobilization medium that is frozen to provide a solidified block of bone and immobilization medium prior to layer cutting, the rejection is applicable to the instant case. Applicants' selective reading of Boyce et al. ignores the teachings of the references of Dowd and Aaron. There is no requirement for Boyce et al. to teach that which is clearly taught by other references. In the instant case, each and every method step is disclosed in prior art that is intended for preparing bone particle as discussed above. Further, given that prior art teaches milling of bone and immersion medium could be accomplished both as slurry and in frozen state. One of ordinary skill in the art would recognize that the cutting of bone is best carried out with a frozen solidified block of bone and immobilization medium for the reasons described in Aaron et al. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the method steps known in prior art to subdivide the frozen immobilization medium and bone prior to freeze drying using the method known in art (see Dowd) for the reasons disclosed in Aaron, in the method of subdividing bone, with a reasonable expectation of success, at the time of the instant invention. Applicants should note that MPEP 2144.04 Ex parte Rubin ,

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128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); *In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.). In absence of any criticality of a method step or any other secondary consideration, it would have been obvious for one of ordinary skill in the art to combine the teaching of known method steps to improve efficient cutting of bone specimen as claimed in the instant application.

Therefore, in view of the fact patterns of the instant case, and the ground of rejection outlined by the examiner, applicant's arguments are not compelling and do not overcome the rejection of record.

Should Applicant provide evidence in support of the criticality of the order of method steps claimed or any other appropriate secondary consideration, the above obviousness rejection may be overcome pending further consideration.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anoop Singh/
Examiner, Art Unit 1632